Reprinted from the Scientific American
Vo. 194, No. 5 May, 1956

1956 ✓ (53)

# The Eye and the Brain

*If the optic nerve of a newt is cut and its eye is turned through 180 degrees, the nerve regenerates and the animal sees upside down. Such results deeply affect our picture of how the nervous system develops*

by R. W. Sperry

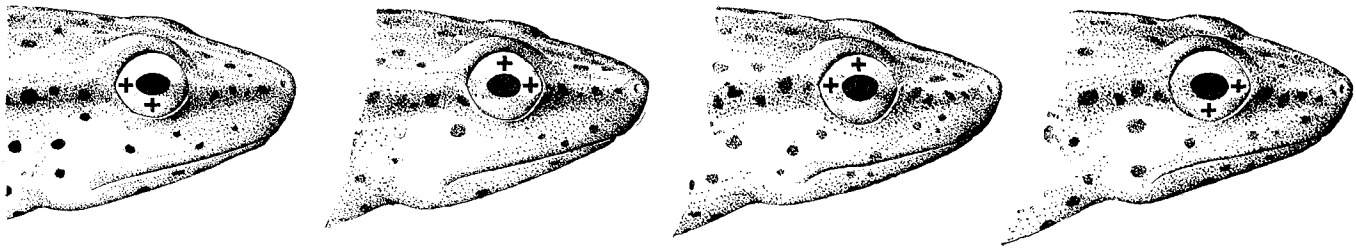
Probably no question about the behavior of living things holds greater general interest than the age-old issue: Heredity versus Learning. And none perhaps is more difficult to investigate in any clear-cut way. Most behavior has elements of both inheritance and training; yet each must make a distinct contribution. The problem is to separate the contributions. We can take vision as a case in point. An animal, it is often said, must learn to see. It is born with eyes, but it matures in the use of them. The question is: Just where does its inborn seeing ability end and learning begin? To put the matter another way: Exactly what equipment and instinctive skills are we born with?

This article is an account of experiments which have given some new insight into the heredity-learning question. The behavior studied is vision, and the story begins 31 years ago.

In 1925 Robert Matthey, a zoologist of the University of Geneva, delivered to the Society of Biology in Paris an astonishing report. He had severed the optic nerve in adult newts, or salamanders, and they had later recovered their vision! New nerve fibers had sprouted from the cut stump and had managed to grow back to the visual centers of the brain. That an adult animal could regenerate the optic nerve (and even, as Matthey reported later, the retina of the eye) was surprising enough, but that it could also re-establish the complex network of nerve-fiber connections between the eye and a multitude of precisely located points in the brain seemed to border on the incredible. And yet this was the only possible explanation, for without question the newts had regained normal vision. They would stalk a moving worm separated from them by a glass wall in their aquarium; they were able to see a small object distinctly and follow its movements accurately.

A long series of confirmations of Matthey's discovery followed. He transplanted an eyeball from one newt to another, with good recovery of vision. Leon S. Stone and his co-workers at Yale University transplanted eyes successfully from one species of salamander to another, and grafted the same eye in four successive individuals in turn, each of which was able to use the eye to regain its vision. Eventually experimenters found that fishes, frogs and toads (but not mammals) also could regenerate the optic nerve and recover vision if the nerve was cut carefully without damage to the main artery to the retina.

The optic nerve of a fish has tens of thousands of fibers, most or all of which must connect with a specific part of the visual area of the brain if the image on the retina is to be projected accurately to the brain. The newt, whose retina is less fine-grained than a fish's, has fewer optic fibers, but still a great many. The system is analogous to a distributor's map with thousands of strings leading from a focal point to thousands of specific spots on the map. How can an animal whose optic fibers have all been cut near the focal point re-establish this intricate and precisely patterned system of connections? Matthey found that the regenerating fibers wound back into the




**EYE OF THE NEWT** was turned in various ways by the experiments described in this article. In A the normal position of the eye is marked with crosses. In B the eye has been turned so that its front-back and up-down axes are inverted. In C the eye on the opposite side of the head has been transplanted to the side shown with its up-down axis inverted. In D the eye on the opposite side of the head has been transplanted to the side shown with its front-back axis inverted. In each case the operation is done on both eyes.

brain in what looked like a hopelessly mixed up snarl. Yet somehow, from this chaos, the original orderly system of communications was restored.

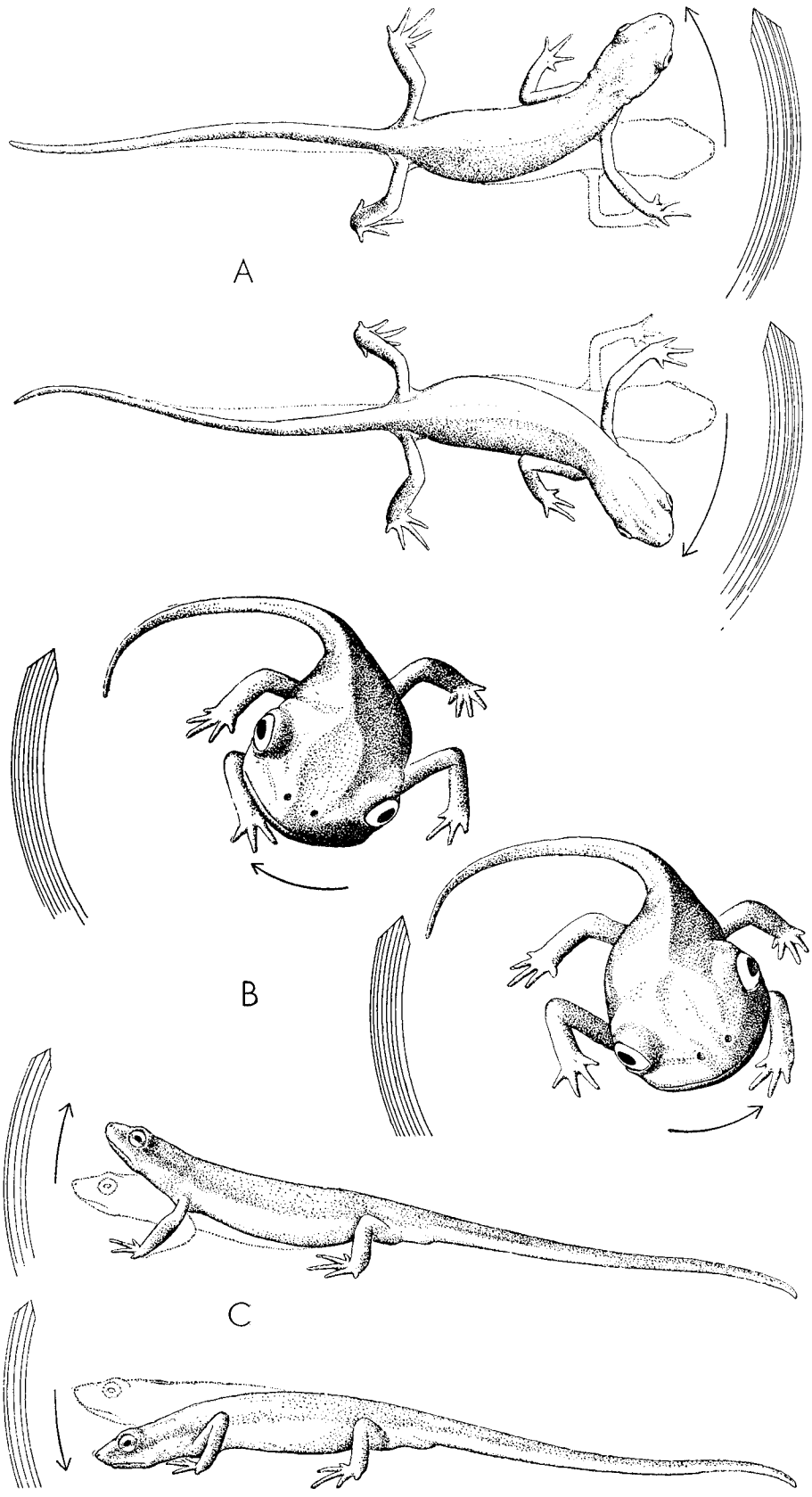
Two possible explanations have been considered. The one that was long regarded as the more plausible is that the connections are formed again by some kind of learning process. According to this theory, as the cut nerve regenerates a host of new fibers, branching and crawling all over the brain, the animal learns through experience to make use of the fiber linkages that happen to be established correctly, and any worthless connections atrophy from disuse.

The second theory is that each fiber is actually specific and somehow manages to arrive at its proper destination in the brain and reform the connection. This implies some kind of affinity, presumably chemical, between each individual optic fiber and matching nerve cells in the brain's visual lobe. The idea that each of the many thousands of nerve fibers involved has a different character seemed so fantastic that it was not very widely accepted.

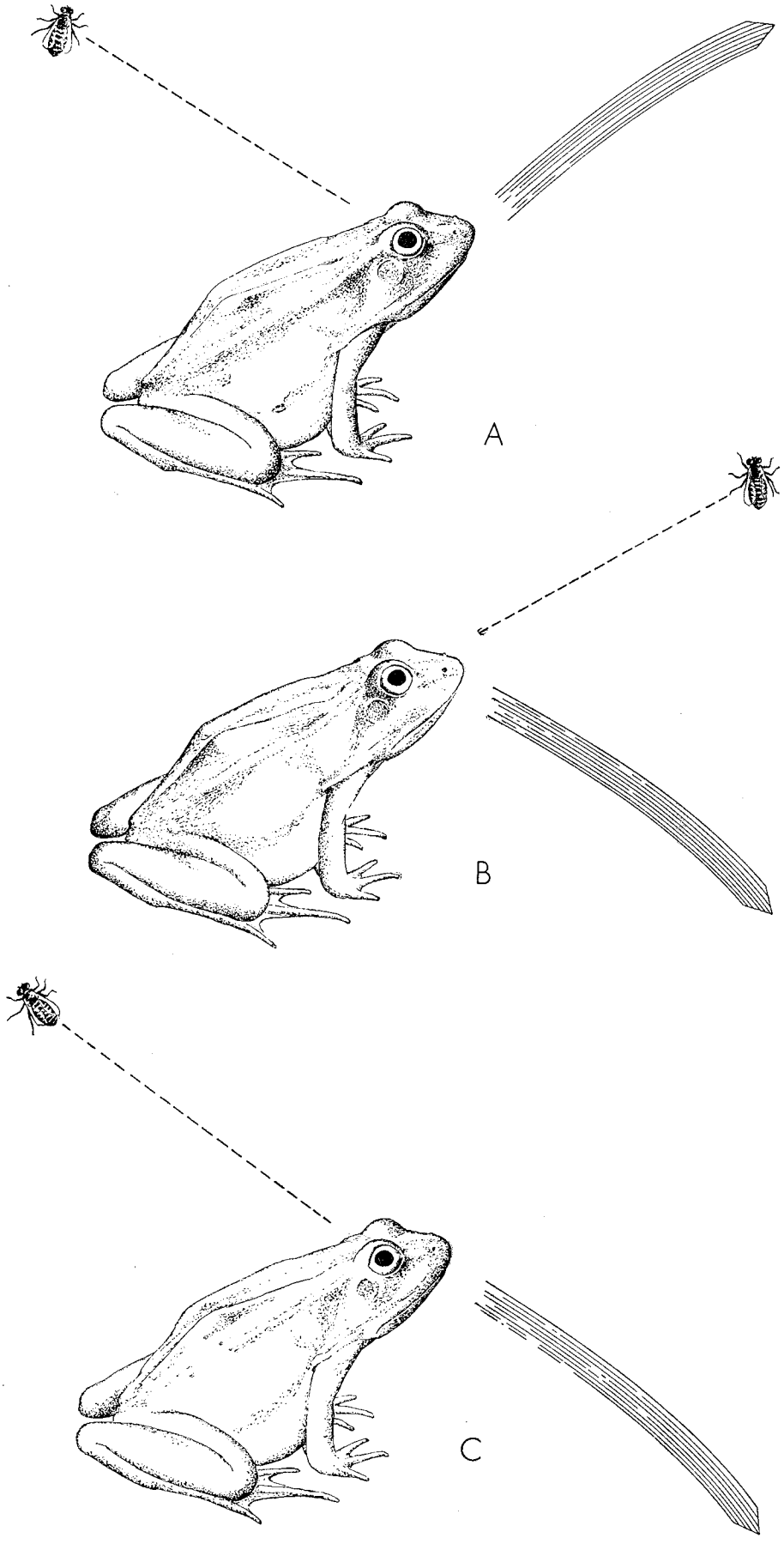
These were the questions we undertook to test: Does the newt relearn to see, or does its heredity, forming and organizing its regenerated fibers according to a genetic pattern, automatically restore orderly vision?

Our first experiment was to turn the eye of the newt upside down—to find out whether this rotation of the eyeball would produce upside-down vision, and if so, whether the inverted vision could be corrected by experience and training. We cut the eyeball free of the eyelids and muscles, leaving the optic nerve and main blood vessels intact, then turned the eyeball by 180 degrees. The tissues rapidly healed and the eyeball stayed fixed in the new position.

The vision of animals operated on this way was then tested. Their responses showed very clearly that their vision was reversed. When a piece of bait was held above the newt's head, it would begin digging into the pebbles and sand on the bottom of the aquarium. When the lure was presented in front of its head, it would turn around and start searching in the rear; when the bait was behind it, the animal would lunge forward. (Since its eyes are on the side of the head, a newt can see objects behind it.) As color-adapting animals, the newts with upside-down eyes even adjusted their color to the brightness above them instead of to the dark background of the aquarium bottom. Besides seeing everything up-




**RESPONSE OF THE NEWT** to moving objects varies with the operations depicted on the opposite page. The first newt in each of the three pairs of animals on this page is normal. When an object (*thick arrows*) is moved past the newt, the animal turns its head in the same direction (*thin arrows*). The second newt in each pair represents the behavior of the animal after one or more of the operations. The response of the second newt in A corresponds to operations B and D on the opposite page; in B, to operations B and C; in C, to C and D.




SAME OPERATIONS ON A FROG produce these effects when the animal strikes at a fly. In A the fly is above and behind a frog whose eyes have been turned by operation D on page 48; the animal strikes in the direction shown by the thick arrow. In B the eyes of the frog have been turned by operation C. In C the eyes of the frog have been turned by operation B.

side down and backward, the animals kept turning in circles, as if the whole visual field appeared to be whirling about them. Human subjects who have worn experimental lenses that invert the visual field have reported that any movement of the head or eyes tends to make everything seem to whirl around them.

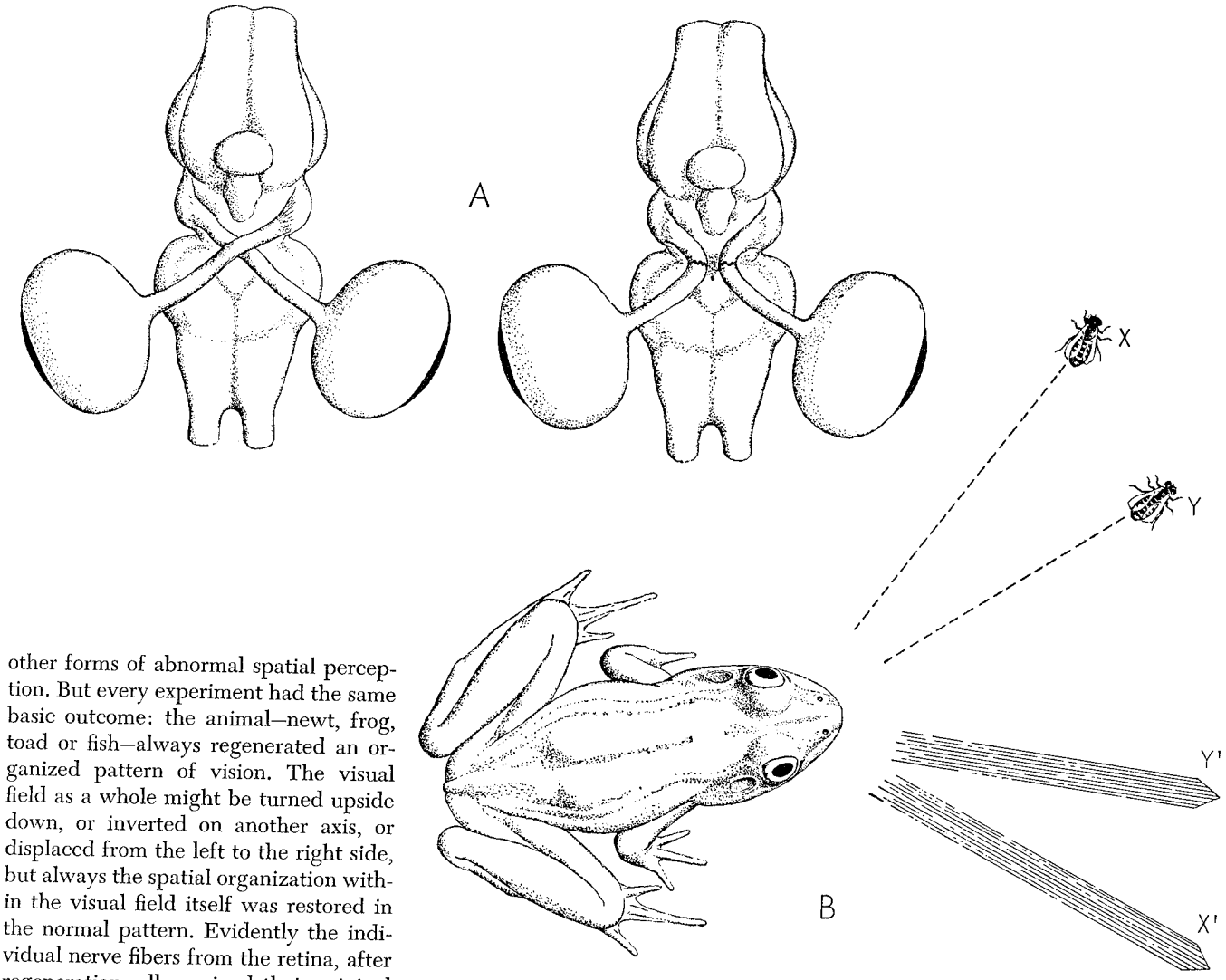
The operated newts never relearned to see normally during the experiment. Some were kept with their eyes inverted for as long as two years, but showed no significant improvement. However, when rotated eyes were turned back to the normal position by surgery, the animals at once resumed normal behavior. There was no evidence that their long experience with inverted vision had brought about any change in the functioning of the central nervous system.

A second experiment bore out further the now growing suspicion that learning probably was not responsible for the recovery of vision by newts whose optic nerves had been cut. This time we rotated the eyeball and severed the optic nerve as well. The object was to find out whether the regenerating nerve fibers would give the newt normal vision, inverted vision or just a confused blur.

During the period of nerve regeneration the animals were blind. The first visual responses began to reappear about 25 to 30 days after the nerve had been cut. From the beginning these responses were systematically reversed in the same way as those produced by eye rotation alone. In other words, the animals again responded as if everything was seen upside down and backward. In these animals also the reversed vision remained permanently uncorrected by experience.

In another series of experiments we cut the optic nerves of the two eyes and switched their connections to the brain. Normally each optic nerve crosses to the side of the brain opposite the eye. We connected the cut nerve to the brain lobe on the same side. The result was to make the animals behave after regeneration as if the right and left halves of the visual field were reversed. That is, the animals responded to anything seen through one eye as if it were being viewed through the other eye. This switch too was permanent, uncorrected by experience. Frogs and toads responded to the experiment in the same way as newts.

By rotating the eyeball less than 180 degrees (*e.g.*, a 90-degree turn), and by combining eye transplantation from one side to the other with various degrees of rotation, we produced many




**OPERATION ON THE OPTIC NERVES** of a frog produced the effect shown at the lower right. At upper left the eyes of the frog are joined to the brain by the optic nerves. In the operation, which is depicted at top center, the nerves were cut and rejoined so that they did not cross. When a fly was at X, the frog struck at X'; when it was at Y, the frog struck at Y'.

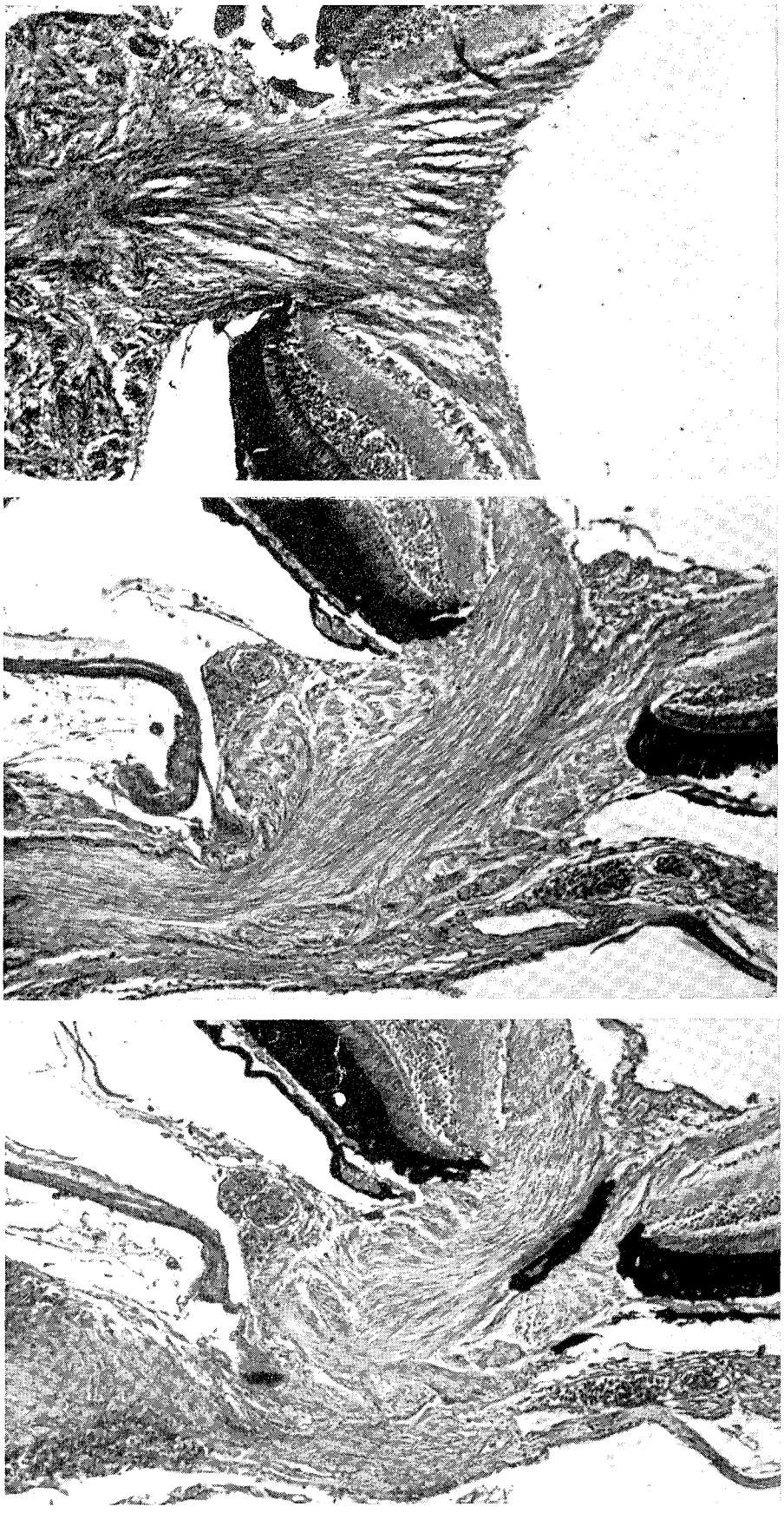
other forms of abnormal spatial perception. But every experiment had the same basic outcome: the animal—newt, frog, toad or fish—always regenerated an organized pattern of vision. The visual field as a whole might be turned upside down, or inverted on another axis, or displaced from the left to the right side, but always the spatial organization within the visual field itself was restored in the normal pattern. Evidently the individual nerve fibers from the retina, after regeneration, all regained their original relative spatial functions in projecting the picture to the brain.

This orderly restoration of the spatial relations could hardly be based on any kind of learning or adaptation, under the conditions of our experiments. Animals don't *learn* to see things upside down and backward or reversed from left to right: reversed vision is more disadvantageous than no vision at all. The results clearly demonstrated that the orderly recovery of correct functional relations on the part of the ingrowing fibers was not achieved through function and experience, but rather was predetermined in the growth process itself.

Apparently the tangle of regenerating fibers was sorted out in the brain so as to restore the orderly maplike projection of the retina upon the optic lobe. If we destroyed a small part of the optic lobe after such regeneration, the animal had a blind spot in the corresponding part of its visual field, just as would be the case in normal animals. It was as if each regenerated fiber did indeed make a connection with a spot in the brain matching a corresponding spot in the retina.

It follows that optic fibers arising from different points in the retina must differ from one another in some way. If the ingrowing optic fibers were indistinguishable from one another, there would be no way in which they could re-establish their different functional connections in an orderly pattern. Each optic fiber must be endowed with some quality, presumably chemical, that marks it as having originated from a particular spot of the retinal field. And the matching spot at its terminus in the brain must have an exactly complementary quality. Presumably an ingrowing fiber will attach itself only to the particular brain cells that match its chemical flavor, so to speak. This chemical specificity seems to lie, as certain further experiments indicate, in a biaxial type of differentiation which produces unique arrays of chemical properties at the junction places.

Such chemical matching would account for recognition on contact, but how does a fiber find its way to its destination? There is good reason to believe that the regenerating fibers employ a shotgun approach. Each fiber puts forth many branches as it grows into the brain, and the brain cells likewise have widespreading branches. Thus the chances are exceedingly good that a given fiber will eventually make contact with its partner cells. We can picture the advancing tip of a fiber making a host of contacts as it invades the dense tangle of brain cells and their treelike expansions. The great majority of these contacts come to nothing, but eventually the growing tip encounters a type of cell surface for which it has a specific chemical affinity and to which it adheres. A chemical reaction then causes the fiber tip to stop advancing and to form a lasting functional union with the group of cells, presumably roughly circular in



OPTIC NERVE of *Bathygobius soporator*, a fish of the goby family, was cut and allowed to regenerate. The regenerated nerve is shown in these three photomicrographic sections. In each photograph the eye is toward the right and the nerve runs from right to left. The top photograph shows a section of one nerve; the bottom two photographs show different sections of the same nerve. In all three sections the nerve fibers are tangled. Despite this apparent disorganization the fishes from which the sections were taken could see normally.

formation, which constitutes the spot in the brain matching the fiber's source spot in the retina.

The experiments on vision have been found to apply equally to other parts of the central nervous system. Normal function can be recovered through regeneration by general sensory nerves in the spinal cord, by the vestibular nerve in the ear mediating the sense of equilibrium and by other sensory and motor nerve circuits.

All the experiments point to one conclusion: the theory of inherent chemical affinities among the nerve fibers and cells is able to account for the kinds of behavior tested better than any hypothetical mechanism based on experience and learning. There is no direct proof of the theory, for no one has yet seen evidence of the chemical affinity type of reaction among nerves under the microscope. But an ever-growing accumulation of experimental findings continues to add support to the chemical theory.

We return to our original question: How big a role does heredity play in behavior? The experiments cited here show that in the lower vertebrates, at least, many features of visual perception—the sense of direction and location in space, the organization of patterns, the sense of position of the visual field as a whole, the perception of motion, and the like—are built into the organism and do not have to be learned. More general experiments suggest that the organization of pathways and associations in the central nervous system must be ascribed for the most part to inherent developmental patterning, not to experience. Of the thousands of circuit connections in the brain that have been described, not one can demonstrably be attributed to learning. Whatever the neural changes induced in the brain by experience, they are extremely inconspicuous. In the higher animals they are probably located mainly in the more remote byways of the cerebral cortex. In any case they are superimposed upon an already elaborate innate organization.

The whole idea of instincts and the inheritance of behavior traits is becoming much more palatable than it was 15 years ago, when we lacked a satisfactory basis for explaining the organization of inborn behavior. Today we can give more weight to heredity than we did then. Every animal comes into the world with inherited behavior patterns of its species. Much of its behavior is a product of evolution, just as its biological structure is.